Ten-year trends of syphilis in sero-surveillance of pregnant women in Rwanda and correlates of syphilis-HIV co-infection

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Abstract

Syphilis can be transmitted by pregnant women to their children and is a public health problem in Africa. A cross-sectional survey was conducted in 24 antenatal clinics from 2002 to 2003 and increased to 30 sites from 2005 to 2011. Participants were tested for syphilis and HIV. Multi-variate logistic regression was performed to identify risks associated with syphilis and its co-infection with HIV. Results showed that syphilis decreased from 3.8% in 2002 to 2.0% in 2011. Syphilis in the HIV-infected participants increased from 6.0% in 2002 to 10.8% in 2011, but decreased from 3.7% to 1.7% in the HIV-negative participants. In 2011, syphilis in urban participants was 2.7% and 1.4% in rural ones. HIV-infected participants screened positive for syphilis more frequently in both rural (aOR=3.64 [95% CI: 1.56%–8.51%]) and urban areas (aOR=7.26 [95% CI: 5.04%–10.46%]). Older participants (25–49 years) residing in urban areas (aOR=0.43[95% CI: 0.32%–0.58%]) and women with secondary or high education (aOR=0.35[95% CI: 0.20%–0.62%]) were less likely to screen positive for syphilis. HIV-syphilis co-infection was more likely in women residing in urban areas (aOR=8.32[95% CI: 3.54%–19.56%]), but less likely in women with secondary/high education (aOR=0.11[95% CI: 0.01%–0.77%]). In conclusion, syphilis increased in HIV-positive pregnant women, but decreased in HIV-negative women. Positive HIV status and young age were associated risks for syphilis. HIV-syphilis co-infection was associated with a lower level of education and urban residence.

Keywords

Syphilis surveillance; prevalence; HIV co-infection; Rwanda; risk factors

Introduction

Among adults, the estimated number of syphilis infections globally was 36.4 million in 2008, and the incidence of syphilis was 10.6 million cases per year.[1] The estimated incidence in Africa was 3.41 million cases per year,[1] making syphilis a significant public health problem in the region.

The rate of vertical transmission of syphilis from mother to child approaches 100% in early stage disease. [2,3] Congenital syphilis carries a high mortality, and interventions to diagnose and treat syphilis in pregnancy are critical. Worldwide, the estimated number of pregnant women infected with syphilis is 1.36 million, and of these, 80% attended antenatal clinics (ANCs). In Africa, the estimated number of syphilis-infected pregnant women is 535,203 (39.3%).[4]

In Tanzania, the prevalence of any adverse outcome of the pregnancy is 11.0% among pregnant women that screen negative for syphilis compared to 49.0% for those that screen positive for syphilis,[5] and the reported rates of congenital syphilis range from 2.0% to 68.0% among infants born to pregnant women who did not receive syphilis screening and treatment until the third trimester.[6]

Syphilis and HIV infections mutually facilitate their transmission and therefore there is a significant association between these diseases. Ulcerations from syphilis in the genital area provide an entry point for HIV acquisition due to disruption of the natural mucosal and epithelial barrier's integrity.[5] Syphilis has been shown to increase the risk of HIV infection by three-to five-fold.[6] With the HIV pandemic, the prevalence of primary and secondary syphilis has increased in some countries.[7] Notable differences in syphilis prevalence between HIV-positive and HIV-negative persons have been documented in Africa.[8] In Zambia, the prevalence of syphilis is 1.9 times higher in HIV-positive people compared to those who are HIV-negative.[9] Similarly, in Nigeria, the prevalence of syphilis is 14.0% among HIV-infected people and 2.0% among HIV-negative individuals.[10]

The natural history of syphilis is modified by HIV infection. The clinical evolution is shortened and aggravated with an increased risk of neuro-syphilis.[7,11,12] The prevalence of syphilis infection in HIV-positive patients who are immunosuppressed is higher than the prevalence of syphilis infection in HIV-negative individuals.[7,13]

Syphilis and HIV continue to be significant problems in Rwanda. Given the high number of cases of both syphilis and HIV infections in the country, HIV and syphilis sero-surveillance was implemented in ANC sentinel sites in 2002. The aim of this paper is to describe the prevalence of syphilis among pregnant women using ANC sentinel sites over a ten-year period, the associated risk factors and trends.

Methodology

Study design

To determine trends of syphilis prevalence over a ten-year period, data from consecutive ANC cross-sectional surveys conducted in 2002, 2003, 2005, 2007, and 2011 were examined. Similar sampling procedures were used in the earlier years and changed in 2011 due to ethical reasons. From 2002 to 2007, unlinked and anonymous methods (identifiers of participants were removed and there was no link of collected information to individuals) using blood samples collected for routine RPR tests for all pregnant women attending ANC services were used. In 2011, the linked method (using a personal identifier to track individuals) was used.

Setting and sites

The number of sentinel sites in 2002 and 2003 was 24, but increased to 30 from 2005; 14 sites were located in urban areas and 16 were in rural areas. Each province had at least two urban and two rural sites except for Kigali, which is represented by three urban sites. To be included in the survey, a site had to have at least 80 new pregnant women enrolled at an ANC per month, be geographically accessible, have at least one midwife, experienced maternity or ANC nurse, and at least one laboratory technician.

Sentinel population

Participants were pregnant women 15–49 years old presenting for the first time for their current pregnancy for ANC and prevention of mother to child transmission (PMTCT) services during the data collection period and voluntarily agreeing to a venous blood draw for HIV and syphilis testing. Leftover blood samples presented for a routine syphilis test were used. The demographic and other data from the patient files were retained but unlinked from the personally identifiable information. In 2011, pregnant women 18 years and above were tested after giving consent. Women younger than 18 years who were accompanied by a responsible adult signed an assent form to participate in the survey. The calculated minimum sample size required to detect a difference in proportions ranging from 3 to 7% per sentinel site at an alpha of 0.05 and power of 0.80 was 13,267.

Laboratory methods

At the health facility level—In 2011, blood samples were collected in Ethylene Diamine Triacetic Acid (EDTA) tubes for HIV rapid testing and rapid plasma reagin (RPR) screening test for syphilis in order to provide results the same day for clinical care at the health facility. Indeterminate RPR tests were retested, and if they remained indeterminate or tested positive, they were confirmed at the National Reference Laboratory (NRL) using a Treponema Pallidum Haemagglutination Assay (TPHA) confirmatory test.

At national reference laboratory—Syphilis testing: In earlier years, RPR test results were used for routine clinical care and for syphilis surveillance in women attending ANCs. In 2011, for study purposes, a confirmatory test using TPHA was used on samples that screened positive on the RPR test.

HIV laboratory testing: HIV Vironostika Uni Form I Ag/Ab, 4th generation was used as a screening test. All samples with non-reactive results to Vironostika HIV Uni Form I Ag/Ab were considered negative. Positive samples from the Vironostika test were followed by a Murex HIV antigen/antibody combination test for confirmation. Samples were considered positive if they were reactive to both Murex and Vironostika tests. If there was a discrepancy (i.e. Vironostika reactive and Murex non-reactive), the samples were confirmed by Enzygnost.

External quality control: A random selection of 5% in negative samples and 10% of positive samples were stored at NRL at a temperature of minus 70 °C for ELISA testing for quality control. The feedback from NRL was sent to health facilities and updated in the patient charts. We therefore did not have any outstanding indeterminate HIV or syphilis test results to address in the analysis.

Data collection

There were three focal persons per sentinel site, consisting of the director of the health facility, an ANC staff, and a laboratory technician. All received five-day training on the protocol, laboratory techniques related to the surveillance, standard operating procedures of data collection and blood sample collection.

For all consecutive surveys, data were collected using a surveillance questionnaire for all eligible pregnant women. The surveillance form was used to collect socio-demographic information administered by trained ANC-PMTCT staff. Forms were maintained at the sentinel sites and transported to the Rwanda Biomedical Center (RBC) approximately every two weeks at the time of regular site visits. Surveillance forms and laboratory results were double-entered using EpiInfo (CDC, Atlanta, GA, USA).

Data analysis

Data were analysed using STATA software (StataCorp LP, College Station, TX, USA). Data quality assurance measures included writing a consistency check code to avoid or minimise data entry and management errors. Syphilis prevalence trends were evaluated using data from the 24 sentinel sites that were surveyed in all the five sero-surveillance surveys. Only data from the 2011 survey were used for multi-variate logistic regression modelling. Data were pooled across all sites for analysis. Odds ratios (OR) of syphilis screening results were estimated using bi-variate analyses. Factors that were associated with syphilis infection in the bivariate analysis at the 0.1 significance level were considered when developing the final multi-variable model. To identify potential risk factors, a multi-variate analysis using a backward elimination method was used. The associations of missing values for key variables used in the regression analyses were assessed by fitting indicator variables for missing values for each variable with the outcome and were tested using a maximum likelihood test and found not to be associated with the outcome (missing at random). The prevalence of syphilis screening among pregnant women was estimated at 95% confidence intervals (CI). The risk factors for syphilis infection were determined using co-variates fitted in the multi-variable logistic regression analysis: age, HIV infection, marital status, education level,

occupation, residence, and parity. A likelihood ratio test was used to check for interactions and in determining the best multi-variable model for the data.

Ethical considerations

Surveillance conducted prior to 2011 was unlinked and conducted anonymously according to UNAIDS/WHO guidelines. In 2011, blood specimen and interview-based data collection were only performed on eligible participants who provided informed consent. The survey protocols were reviewed and approved by the Centers for Disease Control and Prevention (CDC) and by the Rwandan National Ethics committee.

Results

The overall prevalence of syphilis determined by the RPR test decreased significantly from 3.8% in 2002 to 2.0% in 2011 ($p<0.01$; Table 1). This decreasing trend of syphilis prevalence was observed in the majority of socio-demographic characteristics apart from those who were cohabiting or divorced, housewives and business-women, women with a university education, and the youngest (15–19 years) and oldest pregnant women (>39 years), where there was no significant change ($p>0.05$).

Analysed by HIV status, the prevalence of syphilis was always higher among HIV-positive than HIV-negative pregnant women. In HIV-negative pregnant women, the prevalence of syphilis decreased from 3.7% in 2002 to 1.7% in 2011 ($p<0.001$). However, in HIV-positive pregnant women, syphilis prevalence increased from 6.0% in 2002 to 10.8% in 2011 ($p<0.001$). The overall syphilis prevalence among HIV-positive pregnant women was higher compared to HIV-negative in 2002 (respectively 6.0% vs. 3.7%). That difference increased significantly to six times as higher in 2011, from 1.7%; (95% CI: 1.6%–2.0%) in HIV-negative compared to 10.8%; (95% CI: 8.4%–14.5%) in HIV-positive.

There was also a significant decrease in the prevalence of syphilis among married pregnant women from 4.2% in 2002 to 1.7% in 2011 ($p<0.001$), single pregnant women (6.8% to 1.8%, $p<0.001$), pregnant women residing in rural areas (3.1% to 1.4%, $p<0.001$) and those residing in urban areas (4.6% to 2.7%, $p<0.001$). In almost all surveys, the prevalence of syphilis in urban pregnant women was higher than the prevalence of syphilis from rural pregnant women (Table 1).

In 2011, 279 (2.1%) out of 13,292 samples screened positive for syphilis using the RPR test. TPHA as confirmatory test was performed on 270 RPR-positive samples and 225 (83.3%) were confirmed positive using the TPHA test (Table 2). In general, TPHA positivity from those screened positive by RPR was consistent in all socio-demographic characteristics.

Socio-demographic factors associated with a positive screening for syphilis were analysed, stratified by residence (rural/urban). Age, marital status, education level, occupation, and number of pregnancies were considered in determining the factors associated with screening syphilis positive during the 2011 survey. There was significant interaction in the relationship between age and syphilis in the urban compared to rural population ($p<0.001$). For pregnant women residing in rural areas, after adjusting for the effects of other variables in the multi-

variable analysis, pregnant women in the age-group 25–49 were more likely to be infected with syphilis than those in the age-group 15–24 years (aOR=1.53 [95% CI: 0.95%–2.46%]) but attained a borderline significance and being HIV-positive was significantly associated with syphilis infection (aOR=3.64 [95% CI: 1.56%–8.51%]) (Table 3).

For pregnant women residing in urban areas, in the multi-variable model, those 25–49 years of age compared to those 15–24 years of age (aOR=0.43 [95% CI: 0.32%–0.58%]) and those with secondary or high education level compared to illiterate and primary education level (aOR=0.35 [95% CI: 0.20%–0.62%]) had a lower risk of screening syphilis positive. Compared to HIV negativity, HIV positivity was associated with a higher risk of screening syphilis positive (aOR=7.26 [95% CI: 5.04%–10.46%]) (Table 3).

Syphilis and HIV co-infection was analysed. In the multi-variable logistic regression, having secondary and higher levels of education was associated with a lower risk of presenting with both syphilis and HIV co-infection (aOR=0.11; [95% CI: 0.01%–0.77%]) but residing in an urban area was strongly associated with a higher risk of syphilis and HIV co-infection (aOR=8.32; [95% CI: 3.54%–19.56%]) (Table 3).

The prevalence of syphilis among 15–19 years old, married, and those attending ANC for their first pregnancy was eight-fold higher in those who were HIV-positive compared to HIV-negative (p<0.001). Additionally, younger pregnant women with a positive screening test of syphilis were more likely to be found in urban residence than in the rural residence.

Discussion

From 2003 to 2011, the prevalence of syphilis among pregnant women attending ANC in Rwanda decreased from 4.2% to 2.0%. The trend of prevalence of syphilis decreased among HIV-negative pregnant women, but it increased steadily among pregnant HIV-positive women. The TPHA confirmatory test for syphilis infection confirmed 83.3% of positive RPR tests. There was no significant difference between the screening and confirmatory syphilis tests among HIV-positive and HIV-negative pregnant women. Residing in urban areas and having a lower level of education was associated with HIV and syphilis co-infection.

In sub-Saharan African countries, the prevalence of syphilis among pregnant women was estimated to range from 0.6% in Senegal to 14.0% in Equatorial Guinea.[11] The prevalence of syphilis found among pregnant women attending antenatal clinics in Rwanda was among the lowest (2.1%) in sub-Saharan African countries. The prevalence of syphilis among pregnant women in Rwanda was higher in urban than in rural areas. The same observation was found in Zambia where syphilis prevalence was highest among pregnant women residing in urban residence (9.2%) as compared to those residing in rural (7.8%).[9] In contrast, a study conducted in Tanzania found the opposite where syphilis prevalence was highest among pregnant women from remote rural residents (16.0%) compared to urban residents (7.0%).[12]

In this study, the prevalence of syphilis was significantly different among pregnant women in sentinel sites according to their HIV status. The prevalence of syphilis in HIV-negative women has followed a decreasing trend, except for a peak in 2005. However, the opposite

has been observed in the prevalence of syphilis among HIV-positive pregnant women. The overall trend increased, ranging from 6% in 2001 to 11% in 2011. This prevalence was constantly higher among HIV-positive women in all considered socio-demographic characteristics and increased over time. These findings are in contrast with earlier studies from Zambia, South-Africa, and India, which found trends of decreasing syphilis prevalence in HIV-infected pregnant women.[9,14] For example, in South Africa, the prevalence of syphilis varied from 3.2% in 2002 to 1.6% in 2011.[15] In Zambia, it declined from 9.2% in 1998 to 3.2% in 2008.[9] This difference in syphilis trends may be a result of the small and decreasing numbers of HIV-positive pregnant women over time leading to more imprecise estimates, but it may also be due to differences in sexual behaviour, most especially the negotiating power for safer sex in Rwandan women who already know that they are HIV-positive.

Younger pregnant women attending ANC in urban areas, illiterate or pregnant women with primary education level, urban residence and HIV-positive women were more likely to be associated with syphilis infection in a multi-variate analysis. Pregnant women who had attained secondary or higher education levels were less likely to be associated with syphilis infection and HIV-syphilis coinfection. The reason could be the self-efficacy of more educated women in negotiating safe sex and possible other sources of income other than sex work among educated women compared to illiterate ones.[16]

Living in an urban area was a risk factor for both syphilis infection as well as HIV and syphilis coinfection. In our study, HIV prevalence is shown to be higher in urban areas compared to rural areas. This observation is similar to what was reported in the Rwanda Demographic Health Survey (DHS) 2010.[17] Possible reasons that may explain why the HIV and syphilis co-infection appeared higher in urban than in rural areas include: high HIV prevalence in the urban population and a commercial sex worker population with 51.0% HIV prevalence mostly residing in urban areas. Our study found that age plays a role in the prevalence of syphilis and HIV-syphilis co-infection. Syphilis infection was more prevalent in pregnant women between the ages of 15 and 24 than those aged 25–49. The prevalence of syphilis among pregnant women in the rural areas of Tanzania was 1.6%, and was higher (2.4%) among young women.[18,19] This observation may also reflect barriers to accessing effective prevention services, financial constraints, confidentiality concerns, and lack of facilities designed to accommodate the needs of young pregnant women.

This study has several limitations. Although sentinel sites were located in all administrative districts, results from the current study cannot be extrapolated to all pregnant women in the country because sero-surveillance sites are not necessarily a representative sample of all ANC sites in the country. Several sexual risk factors were not collected in these surveys due to the sentinel surveillance nature of our data, and therefore more data are needed on sexual behaviours and sexual partners experience. Data were pooled across all sites for analysis, and therefore site-level variation was not accounted for in the trends analysis. This may have impacted our trends assessment but we believe that these limitations did not significantly affect the final interpretation of study findings.

In conclusion, the data collected from sentinel sites provided useful information to decision makers for prevalence estimates and their trends over time. Sero-surveillance data show that syphilis is still a major public health problem in sentinel sites in Rwanda, and HIV is a major correlate of syphilis infection. Syphilis among HIV-infected pregnant women has increased over time, and therefore efforts to prevent HIV infection would significantly help in preventing syphilis and other STIs. The systematic screening of STIs should be reinforced especially among people living with HIV.

Acknowledgments

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Table 1

Trends of syphilis using the 24 sentinel sites surveyed in all ANC sero-surveys from 2002 to 2011, Rwanda.

Characteristics	2002 N	2002 Syphilis prevalence (%)	2003 N	2003 Syphilis prevalence (%)	2005 N	2005 Syphilis prevalence (%)	2007 N	2007 Syphilis prevalence (%)	2011 N	2011 Syphilis prevalence (%)	p Chi square for trend
Overall prevalence	11,556	3.8	11,452	4.2	10,780	4.1	11,064	2.5	10,580	2.0	<0.01
Median Prevalence (IQR)		3.6 (2.5)		3.6 (2.7)		3.8 (2.9)		2.5 (1.3)		1.8 (1.5)	
Age group (5-year interval)											
15–24 Years	4638	3.8	4537	3.8	4140	4.4	4373	2.4	3945	2.5	<0.001
15–19 Years	837	3.5	823	3.4	637	4.4	724	3.5	692	3.5	0.976
20–24 Years	3801	3.9	3714	3.9	3503	4.5	3649	2.2	3253	2.2	<0.001
25–29 Years	2925	3.9	2796	4.0	2819	3.6	3145	2.2	3232	1.5	<0.001
30–34 Years	2159	3.4	2143	4.8	1969	3.7	1830	2.7	1918	1.6	<0.001
35–39 Years	1183	3.5	1191	4.7	1210	4.4	1166	2.6	1031	2.4	0.008
40–44 Years	529	4.9	614	5.1	497	4.8	413	4.1	333	2.7	0.079
45–49 Years	77	3.9	77	5.2	69	1.5	62	1.6	53	3.8	0.627
HIV status											
Negative	10,951	3.7	10,857	4.1	10,332	3.8	10,585	2.2	10,228	1.7	<0.001
Positive	605	6.0	595	5.7	448	10.5	479	9.2	343	10.8	<0.001
Marital status											
Married	6767	4.2	6326	4.5	4586	3.4	5727	1.8	7254	1.7	<0.001
Cohabiting	4307	2.9	4593	3.5	5456	4.3	4381	3.3	1785	3.5	0.282
Divorced/separated/widow	158	6.3	204	4.9	206	6.8	236	4.2	189	3.2	0.154
Single	309	6.8	310	5.8	519	6.6	709	2.5	1,285	1.8	<0.001
Education level											
Illiterate	3259	4.3	3668	4.1	2835	5.0	2726	3.2	1441	3.5	0.055
Primary	7421	3.6	6986	4.3	7111	3.8	7497	2.3	7802	1.9	<0.001
Secondary	848	3.9	686	3.5	727	3.6	726	1.8	1083	1.0	<0.001
University	28	0.0	112	1.8	107	1.9	75	0.0	152	1.3	0.849
Occupation											
Farmer	9027	3.6	9328	4.3	8656	4.0	9058	2.4	8109	1.9	<0.001

Year	2002		2003		2005		2007		2011		p
Characteristics	N	Syphilis prevalence (%)	N	Syphilis prevalence (%)	N	Syphilis prevalence (%)	N	Syphilis prevalence (%)	N	Syphilis prevalence (%)	Chi square for trend
Housewife	1698	4.5	1244	3.6	1028	4.2	1001	2.7	1030	3.6	0.171
Business	406	3.7	369	4.3	518	5.6	415	2.7	469	3.0	0.202
Other (salaried, student, handcraft, hairdresser, tailor…)	407	4.7	474	4.2	565	3.4	581	2.8	862	0.9	<0.001
Residence											
Urban	5361	4.6	5386	4.9	5163	5.0	5080	2.5	5194	2.7	<0.001
Rural	6195	3.1	6066	3.5	5617	3.2	5984	2.5	5386	1.4	<0.001
Pregnancies											
1	2503	3.8	2406	3.5	2275	3.9	2957	2.0	3225	2.1	<0.001
2–3	3836	3.6	3666	3.6	3486	4.5	3776	2.5	4060	2.1	<0.001
4–5	2679	3.9	2627	4.4	2517	3.6	2377	2.6	1904	1.7	<0.001
>=6	2480	3.8	2665	5.3	2349	4.2	1912	3.1	1093	1.6	<0.001

ANC: attended antenatal clinic; IQR: interquartile range.

Table 2

Syphilis screening and confirmatory test results for all the 30 sites by socio-demographic characteristics, using 2011 ANC survey data, Rwanda.

Socio-demographic characteristics	RPR results			TPHA results		
	Total N	RPR positive n	%	Total N	If RPR positive n	%
Overall	13,292	279	2.1	270	225	83.3
Age group						
15–24 Years	4788	127	2.7	122	107	87.7
…15–19 Years	848	29	3.4	27	23	85.2
…20–24 Years	3940	98	2.5	95	84	88.4
25–29 Years	4063	66	1.6	64	47	73.4
30–34 Years	2502	38	1.5	37	34	91.9
35–39 Years	1349	35	2.6	35	28	80.0
40–44 Years	448	11	2.5	10	8	80.0
45–49 Years	66	2	3.0	2	1	50.0
HIV status						
Negative	12,837	229	1.8	227	186	81.9
Positive	442	50	11.3	43	39	90.7
Marital status						
Single	1468	29	2.0	28	26	92.9
Married	9101	156	1.7	150	119	79.3
Divorced	40	1	2.5	0	0	–
Separated	138	6	4.3	6	5	83.3
Cohabiting	2414	85	3.5	85	74	87.1
Widowed	38	1	2.6	0	0	–
Education level						
Illiterate	1843	66	3.6	64	53	82.8
Primary	9831	194	2.0	189	157	83.1
Secondary	1309	15	1.1	13	12	92.3
University	188	2	1.1	2	1	50.0
Occupation						
Salaried	447	3	0.7	3	2	66.7

Socio-demographic characteristics	RPR results			TPHA results		
	Total N	RPR positive n	%	Total N	If RPR positive n	%
Housewife	1319	51	3.9	47	43	91.5
Farmer	10,277	201	2.0	198	162	81.8
Big trader	78	1	1.3	1	1	100.0
Small trader	466	16	3.4	15	12	80.0
Housemaid	63	2	3.2	1	1	100.0
Student	197	2	1.0	2	2	100.0
Others	313	3	1.0	3	2	66.7
Residence						
Rural	6632	94	1.4	94	67	71.3
Urban	6660	185	2.8	176	158	89.8
Pregnancies						
1 Pregnancy	3977	90	2.3	87	67	77.0
2–3 Pregnancies	5112	108	2.1	103	90	87.4
4–5 Pregnancies	2466	45	1.8	44	35	79.5
6 +Pregnancies	1395	24	1.7	24	21	87.5

ANC: attended antenatal clinic; RPR: rapid plasma regain; TPHA: treponema pallidum haemagglutination assay.

Table 3

Risk factors for syphilis infection and HIV-syphilis co-infection using 2011 ANC survey data, Rwanda.

	Number	Syphilis infection				HIV-syphilis co-infection	
		Rural		Urban		Rural and urban	
		Bivariate OR (95% CI)	Multi-variable aOR (95% CI)	Bivariate OR (95% CI)	Multi-variable aOR (95% CI)	Bivariate OR (95% CI)	Multi-variable aOR (95% CI)
Age group							
15–24 Years	4788	1		1		1	
25–49 Years	8428	1.57 (0.98–2.52)[a]	1.53 (0.95–2.46)	0.48 (0.36–0.64)*	0.43 (0.32–0.58)*	0.72 (0.41–1.26)	–
Marital status							
Single/divorced/ separated/widow	1684	1		1		1	
Married/cohabiting	11,515	1.46 (0.67–3.17)	–	0.90 (0.61–1.34)	–	2.30 (0.71–7.39)	–
Education level							
Illiterate/primary	11,674	1		1		1	
Secondary/high	1497	0.80 (0.29–2.20)	–	0.35 (0.20–0.62)*	0.35 (0.20–0.62)*	0.16 (0.02–1.15)[a]	0.11 (0.01–0.77)*
Occupation							
Salaried	1564	1		1		1	
Not salaried	11,596	0.48 (0.12–1.96)	–	0.64 (0.42–0.98)*	–	1.21 (0.54–2.69)	–
Pregnancies							
1–3 Pregnancies	9089	1		1		1	
4 Pregnancies	3861	1.44 (0.95–2.20)[a]	–	0.59 (0.40–0.88)*	–	0.94 (0.51–1.75)	–
HIV status[b]							
Negative	12,837	1		1			
Positive	442	3.87 (1.66–9.04)*	3.64 (1.56–8.51)*	6.92 (4.83–9.91)*	7.26 (5.04–10.46)*	NA	NA
Residence							
Rural	6632					1	
Urban	6660	NA	NA	NA	NA	7.34 (3.13–17.25)*	8.32 (3.54–19.56)*

ANC: attended antenatal clinic; NA: Not applicable; CI: confidence intervals; OR: odds ratio; aOR: adjusted odds ratio.

Note: (Age × Residence) Interaction term was significant in the syphilis infection outcome model ($p<0.001$).

[a] Borderline.

*b*Not applicable (NA) in the HIV-syphilis co-infection model.

*Significant $p<0.05$.